

Role of CD11c⁺ cells in the Paracoccidioidomycosis outcome

Suelen Silvana dos Santos, Luana Rossato, Grasielle Pereira Jannuzzi, Sandro Rogério de Almeida

Universidade de São Paulo (USP)

Av. Prof. Lineu Prestes, 580 - Cidade Universitária/São Paulo

Paracoccidioidomycosis (PCM) is an endemic disease in Latin America and the most frequent systemic mycosis in Brazil. The dendritic cells (DCs) are antigen-presenting cells able to do the link between innate and adaptive immune response that play a pivotal role in important infections caused by airborne pathogens. During the first 12 hours of PCM infection, lung DCs migrate to lymph nodes and induce a mixed pattern of CD4 T cell cytokines, compatible with a Th1/Th2 response. The aim of this work is to characterize the immunological and cellular profile of mice infected with *P. brasiliensis* after CD11c⁺ cells depletion and how the lack of this population interferes in the infection outcome. We evaluate the depletion of CD11c⁺ cells in C57BL/6.CD11c-DTR mice, after 24 hours of administration of diphtheria toxin (DTX). With 4ng/g of animal, we get almost 80% CD11c⁺ cells reduction in the spleen. After this period, we infected the animals intratracheally with *P. brasiliensis*. After 7 and 15 days we had a CD4⁺ cells reduction in lymph nodes, and a small proliferation of this cells obtained from spleen in response of *P. brasiliensis* antigens, in comparison of not depleted animals. In the absence of CD11c⁺ cells we saw an increase of IL4, IL-6 and IL-10 and a decrease of IL-17 after 7 days of infection. In conclusion, animals without CD11c⁺ during the infection had a different pattern of cytokines and a small lymphocyte specific proliferation and altogether these results showed. Now, we are doing bone marrow (BM) chimeras generated by reconstitution of lethally irradiated wild type (wt) recipient mice with CD11c-DTR BM. In contrast to CD11c-DTR transgenic mice, these chimeras allow us to treat with DTx for prolonged periods of time without adverse side. Moreover, the generation of mixed BM chimeras with wt, mutant and CD11c-DTR transgenic BM can be a powerful means to investigate molecular contributions of DC during the PCM infection.

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